REMARKS/ARGUMENTS

With entry of this amendment, claims 3-7, 9, 11, 16, 18-20, 24-26, 32, 34-44 are pending. Claims 3-7, 9, 11, 16, 18, 24-26, 32 and 34-36 stand allowed. Claims 20, 37, 39, 41 and 43 are currently amended. Support for the claim amendments is provided in the specification, for example, at page 13, lines 19-22; page 16, lines 28-29; page 18, lines 15-29; page 21, lines 15-18; and page 34, lines 32-34. No new matter is added by these amendments. No claim amendment should be construed as acquiescence in any ground of rejection.

Information Disclosure Statement

Applicants submitted a Supplemental Information Disclosure Statement on March 31, 2004. Applicants have not received an initialed copy of that information disclosure statement and also have not received the acknowledged return receipt postcard. A courtesy copy of the Supplemental Information Disclosure Statement with a copy of the return receipt postcard (as filed) is submitted with this amendment. Applicants request the Examiner consider the references and return an initialed copy of the Supplemental Information Disclosure Statement to the Applicants.

Claim Objections

Claims 19 and 20 stand objected to as allegedly reciting the same subject matter. Without acquiescing to the objection, Applicants amend claim 20 to recite the pharmaceutical preparation of claim 19 further comprises a pharmaceutically acceptable carrier. Applicants therefore request reconsideration of the objection of claims 19 and 20.

35 U.S.C. § 112, first paragraph, enablement

Claim 37 stands rejected as allegedly not enabled. The Examiner says the specification does not establish the activity of any peptide consisting of a motif of SEQ ID NO:9, wherein within said motif at least 7 residues of SEQ ID NO:9 are conserved, and does not teach how to use the claimed peptide.

While Applicants believe claim 37 is enabled, to expedite prosecution of the instant application claim 37 is amended to recite that the isolated peptide consists of an epitope of human brain carboxypeptidase B, wherein, within said peptide, at least 7 amino acids of SEQ ID NO:9 are conserved, and wherein the peptide binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. As amended, claim 37 requires that the claimed peptide binds to an antibody that binds to full length brain CPB (SEQ ID NO:2). In other words, the claimed peptides are immunologically cross-reactive with the full-length protein. Such peptides can be recognized by a simple screen to determine that the peptide binds to polyclonal sera to the full-length protein. Any peptide that does so bind can be used for the purpose of generating antibodies to the full length protein. These antibodies are useful for detecting brain CPB.

Further, one skilled in the art would reasonably understand that a peptide comprising SEQ ID NO:9 would comprise a shorter core epitope. The shorter core epitope would also bind to an antibody that binds a brain CPB protein. Methods for identification of core epitopes are well known in the art. No undue experimentation is required to determine a core epitope of a 14-amino acid peptide. Indeed, Matsumoto et al., 2001 (previously considered by the Examiner) identified seven amino acid residues of the 14-amino-acid peptide as an epitope. For these reasons, Applicants respectfully submit that claim 37 is enabled.

Applicants respectfully request the Examiner reconsider and withdraw the rejection of claim 37 under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, first paragraph, written description

Claim 37 stands rejected as allegedly lacking sufficient written description. The Examiner says claim 37 lacks written description because the specification does not contain any disclosure of the function of all of the polypeptides within the genus of peptides. Applicants respectfully disagree.

As noted above, claim 37 has been amended to recite an isolated peptide variant of SEQ ID NO:9 consisting of an epitope of human brain carboxypeptidase B, wherein within said peptide at least 7 amino acids of SEQ ID NO:9 are conserved, and wherein the peptide binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. The peptides have a

common structural feature, being a variant of SEQ ID NO:9, wherein within said peptide at least 7 amino acids of SEQ ID NO:9 are conserved. The peptides also have a common function, consisting of an epitope of human brain carboxypeptidase B and binding to an antibody that binds to a protein having an amino acid sequence of SEQ ID NO:2.

The specification describes that partial peptides of brain CPB can be used as antigens (see page 16, lines 28-29). Partial peptides are described as including at least 7, 8 or 9 residues of a brain CPB (see page 13, lines 19-22). The specification further discloses a reduction to practice of a C-terminal antibody to a 14-amino acid C-terminal peptide having SEQ ID NO:9 (see page 34, lines 32-34). Thus, Applicants submit the specification discloses that a function of such partial peptides is to isolate antibodies that bind to a peptide having SEQ ID NO:9.

Applicants submit the instant claim 37 is analogous to the exemplary claim of Example 14, Product by Function, of the Revised Interim Written Description Guidelines Training materials. Like the exemplary claim, the genus of peptides recited in claim 37 is a discrete, well-defined genus of peptides in which at least 7 amino acids of SEQ ID NO:9 are conserved. Any species of the claim can be readily envisaged. Further, as discussed above, the function of such peptides is well defined, binding to an antibody that binds to a brain CPB protein. Thus, Applicants respectfully submit that the structure and function of claimed genus of peptides is described in the instant specification. Claim 37 is therefore consonant with the Example 14 of the Training Materials, and complies with the written description requirement.

Claims 37-44 stand rejected as allegedly containing subject matter not described in the specification in a way as to reasonably convey that Applicants were possession of the claimed invention at the time the application was filed. In particular, the Examiner says the specification fails to disclose any polypeptide consisting of SEQ ID NO:9, wherein at least seven residues of SEQ ID NO:9 are conserved (as recited in claims 37, 39, 41 and 43). The Examiner also says the specification fails to disclose any polypeptide consisting of SEQ ID NO:9, wherein no more than five residues are replaced, deleted, inserted and/or add (claims 38 and 40). The

Examiner further says the specification fails to disclose any fragment of SEQ ID NO:9 (claims 42 and 44).

The Examiner bears the burden of presenting evidence of reasons why a person skilled in the art would not recognize that the written description provides adequate support for the claims. Written descriptive support for a claim limitation can be express, implied or inherent. MPEP § 2163. Written description for a claim to a genus can be shown by "sufficient description of a representative number of species by actual reduction to practice ... or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." MPEP § 2163(II)(3)(ii).

Applicants submit claims 37-44 are consonant with the exemplary claim of Example 14, Product by Function, of the Revised Interim Written Description Guidelines Training materials, and thus comply with the written description requirement. Applicants respond to the rejection of each of claims 37-44 below.

Amended claim 37 recites an isolated peptide consisting of an epitope of human brain carboxypeptidase B in SEQ ID NO:9, wherein, within said peptide, at least 7 amino acids of SEQ ID NO: 9 are conserved, and wherein the peptide binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. It is possible to envision any variant of SEQ ID NO:9 in which at least 7 amino acid residues are conserved. The variants of SEQ ID NO:9 can be used in the same way as SEQ ID NO:9 itself in generating antibodies to be used in detecting of brain CPB protease. Applicants submit the disclosure of partial peptides and variants thereof, along with Applicants demonstration that SEQ ID NO:9 can be used to prepare antibodies against SEQ ID NO:9, provide sufficient written description for the claimed peptides of claim 37.

As discussed above, amended claim 37 is analogous to the claim in Example 14, Product by Function, of the Revised Interim Written Description Guidelines Training Materials. Amended claim 37 recites both structure (at least 7 amino acids of SEQ ID NO:9 are conserved),

and function (binding to antibodies that bind to SEQ ID NO:2). Further, Example 4 of the specification shows an actual reduction to practice of a peptide that binds to antibodies that bind to a protein having SEQ ID NO:2. The specification describes how variants can be prepared, e.g., by genetic engineering techniques, peptide synthetic methods or digestion of the protein with appropriate peptidases (see Specification at page 13, lines 22-25). Further, the skilled artisan will appreciate that procedures for making peptides with substitutions, deletions, insertions and addition were routine in the art as of the priority date of the instant application. Finally, the specification discloses assays for determining whether the peptide binds to an antibody that binds to SEQ ID NO:2. See, e.g., Specification, Example 4, pages 34-35. Thus, Applicants submit claim 37 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement.

Applicants submit claim 38 satisfies the written description requirement for reasons similar to those for claim 37. Claim 38 is directed to, *inter alia*, an isolated peptide variant of SEQ ID NO:9, wherein no more than five amino acids are replaced, deleted, inserted or added. As discussed above, the specification provides support for partial peptides and polypeptides that have at least 9 amino acids of a human brain CPB protein. Because SEQ ID NO:9 is 14 amino acids long, it is possible to envision any variant of SEQ ID NO:9 in which no more than 5 residues have been replaced, deleted, inserted or added.

Further, as discussed above, the specification describes a function for SEQ ID NO:9 and a method of assaying the function of the partial peptides (e.g., an antibody binding assay). The variants of SEQ ID NO:9 can be used in the same way as SEQ ID NO:9 itself in generating antibodies to be used in detecting of brain CPB protease. Thus, Applicants submit claim 38 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement.

Amended Claim 39 is directed to a method for screening a compound that binds to the protein of claim 35. The method includes contacting a test sample with a peptide, wherein, within said peptide, at least 7 amino acids of SEQ ID NO: 9 are conserved, and wherein the

peptide binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. The peptides recited in claim 39 are the same as the peptides of claim 37. As set forth above for claim 37, the recited peptides comprise a discrete, well-defined genus of peptides, in accordance with Example 14 of the Training Materials. The skilled artisan can readily envisage the members of this genus. Further, the function of the recited peptides, binding to an antibody that binds to a brain CPB protein, is described in the specification, as discussed above for claim 37. Thus, Applicants submit claim 39 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement.

Claim 40 is directed to a method for screening for a compound that binds to a protein of claim 35. The method includes, inter alia, contacting a test sample with a peptide variant of SEQ ID NO:9 consisting of an epitope of human CPB, wherein no more than five amino acids of SEQ ID NO:9 are replaced, deleted, inserted and/or added; wherein the peptide variant binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. The peptides recited in claim 40 are the same as the isolated peptide variants of claim 38. As set forth above for claim 38, the recited peptides comprise a discrete, well-defined genus of peptides, in accordance with Example 14 of the Training Materials. The skilled artisan can readily envisage the members of this genus. Further, the function of the peptide variants, binding to an antibody that binds to a brain CPB protein, is described in the specification, as discussed above for claim 38. Thus, Applicants submit claim 40 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement.

Amended claim 41 is generally directed to an isolated peptide fragment of the protein of claim 35, wherein the peptide fragment comprises a C-terminal region in which at least 7 amino acids of SEQ ID NO: 9 are conserved, wherein the peptide fragment binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. Applicants understand the Examiner's concern to be essentially the same as for claim 37. Applicants submit the skilled artisan can readily envision peptides comprising a fragment of the protein of claim 35. Further, as set forth above for claim 37, the skilled artisan can readily envision any peptide fragment in

which at least 7 amino acids of SEQ ID NO:9 are conserved. The recited peptides comprise a discrete, well-defined genus of peptides, in accordance with Example 14 of the Training Materials. Further, the function of the isolated peptide fragments, binding to an antibody that binds to a brain CPB protein, is described in the specification, as discussed above for claim 37. Thus, Applicants submit claim 41 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement.

Claim 42 is generally directed to an isolated peptide fragment of SEQ ID NO:9, wherein the peptide fragment binds to an antibody to a protein having an amino acid sequence of SEQ ID NO: 2. Claim 42 is directed to peptides ranging from 5 to 14 amino acids of SEQ ID NO:9. Applicants submit the skilled artisan would readily envisage all ten peptides recited in this claim. Further, because the claim specifies the function of the peptide, binding to an antibody that binds to a brain CPB protein, claim 42 is consonant with Example 14 of the Training Materials and complies with the written description requirement.

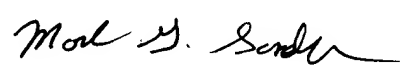
Amended claim 43 is generally directed to a method for screening for a compound that binds to the protein of claim 35. The method includes contacting a test sample with an isolated peptide fragment of the protein of claim 35, wherein the peptide fragment comprises a C-terminal region in which at least 7 amino acids of SEQ ID NO: 9 are conserved, and, wherein the peptide fragment binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. Applicants understand the Examiner's concern to the same as for claim 41. Applicants submit claim 43 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement, for the same reasons as claim 41.

Claim 44 is directed to a method for screening a compound that binds to the protein of claim 35. The method includes contacting a test sample with an isolated peptide fragment of SEQ ID NO:9, wherein the peptide fragment binds to an antibody to a protein having an amino acid sequence of SEQ ID NO:2. Applicants understand the Examiner's concern

to the same as for claim 42. Applicants submit claim 44 is consonant with the Example 14 of the Training Materials, and complies with the written description requirement, for the same reasons as claim 42.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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